ACUTE PARAMETRITIS

Six patients of acute parametritis were treated with sulfanilamid, according to the 80–80–60 plan. Five of these patients became afebrile and symptom free within one week. At this time the previously tender and markedly indurated broad ligaments had become soft and pliable. Tenderness was almost entirely absent. These patients left the hospital in twelve days. No restrictions were placed upon their activities while at home. Reëxamination in the follow-up clinic at one, and at two months failed to show any palpable pelvic pathology. The one patient that failed to respond to therapy had persistent lower abdominal pain and fever, which lasted for six weeks, in spite of large dosages of sulfanilamid totaling over 1,600 grains.

COMPLICATIONS

Anemia occurred in 50 per cent of the patients in this series. The average drop in hemoglobin was 19 per cent Sahli, and the average drop in red blood cells was 1,000,000.

Leucopenia developed in only one patient. The initial white count of 12,000 dropped to 3,400 after 485 grains of sulfanilamid, given according to the 80–80–60 scheme. Toxic symptoms were absent.

Nausea occurred in 40 per cent and vomiting in 20 per cent of the patients. The average quantity of drug producing nausea was found to be in the neighborhood of 340 grains. Administration of sodium bicarbonate with the sulfanilamid tablets helped to reduce nausea in a few cases.

Cyanosis occurred in 35 per cent. If this complication developed it usually appeared early in the course of therapy. The average total dosage causing cyanosis was found to be approximately 200 grains.

Cerebral symptoms, including headache, dizziness, disorientation, etc., were noted in 32 per cent of the patients.

Sulfanilamid in total dosages varying from 60 to 420 grains caused chills and fever in about 1 per cent of patients. Some of these temperatures reached 104 degrees. If a patient once developed chills and fever from the drug, small doses would invariably cause reappearance of the symptoms, even when given some five or six days after the sulfanilamid had been discontinued.

One patient developed dermatitis. The skin lesion was a fine macular rash which was generalized and not limited to the exposed portions of the body. This rash disappeared thirty-six hours after sulfanilamid therapy was discontinued.

CONCLUSIONS

The foregoing data suggest that sulfanilamid therapy in acute salpingo-oöphoritis is more effective during the initial attack than at any other time in the course of the disease. In our series a single week of sulfanilamid treatment produced apparent cures in 100 per cent of the initial patients not having demonstrable inflammatory masses.

Likewise, sulfanilamid appears to have definite therapeutic value in most cases of recurrent acute salpingo-oöphoritis unaccompanied by inflammatory masses. Our results show that 100 per cent of such patients were rendered afebrile and symptom free after ten days therapy; however, adnexal thickening and tenderness persisted for at least three weeks.

The beneficial effects from sulfanilamid therapy, in either initial or recurrent acute salpingo-oöphoritis, were found to be much less striking in those patients having palpable inflammatory masses. Conversely, sulfanilamid was found to produce but little if any improvement in adnexal masses.

Acute gonococcal cervicitis seems to respond excellently to sulfanilamid, but such therapy apparently has little value in chronic cervicitis.

Five out of six cases of acute parametritis were afebrile, and without palpable pathology after the completion of but one week of sulfanilamid therapy. Such evidence speaks for the value of sulfanilamid in the treatment of acute parametritis.

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DISCUSSION

H. N. SHAW, M.D. (901 Pacific Mutual Building, Los Angeles).—Our experience with sulfanilamid has been very similar to that of the author's.

It has given almost miraculous results in cases of acute gonorrheal salpingo-oöphoritis. A case with high fever and frightful pain which, under former methods, would require four to six weeks of bed rest before almost inevitable surgery, is now free from fever and discomfort within two or three days. The majority of these cases escape surgery. In exacerbations of old infections it renders them safe for surgery far sooner than any other method.

Recently, we removed the uterus and both tubes in a case where we expected to find tuberculous salpingitis. Smears made in surgery, and the microscopic sections, showed streptococcus. The patient developed a typical cellulitis in the broad ligaments, but this became soft and pliable in three or four days under sulfanilamid.

It is not a drug to be used without careful supervision. Reports from various clinics of deaths following relatively small doses indicate that some patients have a dangerous idiosyncrasy to sulfanilamid. Under a careful regimen, it has proved an invaluable method in the treatment of pelvic infections.

SULFANILAMID: ITS USE IN THE TREATMENT OF GONORRHEA OF THE LOWER GENITAL TRACT OF THE FEMALE*

By ARNOLD MANOR, M. D.
San Francisco

DISCUSSION *by Norman H. Williams, M. D., Los Angeles.*

ALTHOUGH for several years European medical journals have called attention to the beneficial effect of sulfanilamid on clinical and experimentally produced infections by the beta hemolytic streptococcus, the drug was not introduced into this country until the latter part of 1936. Since then, however, its use in combating various infectious diseases has rapidly increased, as evidenced by the numerous reports appearing in our medical literature during the past year.

Long and Bliss[1] were the first in this country (January, 1937), to confirm the experimental results of European investigators, who found that

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sulfanilamid produced a very favorable reaction in mice infected with many times the lethal dose of beta hemolytic streptococci.

In 1936, Buttle and his coworkers[2] reported that sulfanilamid had a marked protective action against meningococcic infection in mice, and the following year Proom [3] confirmed their results. Schwentker[4] applied this observation clinically, and reported favorably on the effect of this drug in the treatment of meningococcic meningitis. As a result of this work, and because of the close biologic relationship between the meningococcus and the gonococcus, Long suggested the possibility of its therapeutic application in the treatment of gonorrhea. Dees and Colston,[5] acting upon this suggestion, made a preliminary report in May, 1937, on the use of sulfanilamid in the treatment of this infection in the male. The high percentage of successful results reported by them led us to employ it in the treatment of gonorrhea in the female.

STUDIES BY THE AUTHOR

In the study undertaken by us, we are primarily concerned with the effect of sulfanilamid on gonorrhea involving the cervix, Skene's or Bartholin's glands, and only patients in whom the gonococcus could be positively identified are included. In order to evaluate our results properly, no treatment other than the sulfanilamid was used, except where a particularly profuse and annoying discharge necessitated a cleansing douche. Most of the patients were cared for in our out-patient clinic, although a few were hospitalized because of associated severe pelvic inflammatory disease. At the beginning of treatment a blood Wassermann determination and complete blood count were done on each patient, and the red cell count and hemoglobin determination were checked weekly during the course of therapy. During the period of observation, which was four weeks or longer, alcohol and sex activity were forbidden, but no other restrictions were imposed. Patients reported at the clinic twice weekly for smears, and at each visit symptoms attributable to the drug were carefully recorded.

DOSAGE PROCEDURE

A dosage system similar to that suggested by Colston and Dees was employed by us, as follows: 1.2 grams four times daily for two days, 0.9 gram four times daily for three days, then 0.3 gram four times daily until a total of 30 grams had been given. The time required for this dosage is thirteen days. Later, a group of patients were treated with smaller amounts, using 0.6 gram three times daily until a total of 15 to 30 grams had been given. The time required for the maximum dose at this rate is seventeen days.

CLINICAL MATERIAL FOR THE STUDY

The total number of patients included in our study was thirty-three. Of this number, twenty-three, or 70 per cent, were cured; seven, or 21 per cent, had a relapse; and three, or 9 per cent, failed to respond to treatment. Of the seven whom we thought cured, but who returned with a recurrence or reinfection, five were cured following a subsequent course of treatment, and have remained so, and two were lost track of.

Twelve of the thirty-three patients received small daily doses. In this group, eight, or 67 per cent, were cured; one, or 8 per cent, had a relapse; and three, or 25 per cent, failed to show any improvement.

In the cases considered cured, the smears became negative in from three to ten days after the beginning of treatment, the usual time being three to four days. The one patient who was apparently cured, but who suffered a relapse, was later given larger doses, following which her smears became negative, and have remained so for more than four weeks. One of the three who did not respond to the small doses was cured by the large doses, while the other two failed to be influenced by either.

Twenty-five patients were treated with large daily doses, and of these, sixteen, or 64 per cent. were cured; six, or 24 per cent, had a relapse; and three, or 12 per cent, failed to show any response. The smears of those cured in this group became negative in two to ten days (most often in three to five days), and remained so. In most instances the discharge changed in character and amount from profuse and purulent to scant and mucoid. Relapse occurred in the six patients in from four to eight weeks following the beginning of treatment. Four of these (16 per cent), were cured by a subsequent course of treatment and have remained so, and the other two were not followed. Two of the three patients who showed no response in this group were also not influenced by the smaller dosage.

Evidence of intrapelvic inflammatory disease was noted in twelve (36 per cent), patients. Some improvement, which varied markedly in degree, was observed in the majority of these women. The impression obtained was that the improvement was more marked in patients in whom the inflammatory condition was acute or quite recent than in those in whom it was chronic. In none of the patients did a pelvic inflammatory process develop after the beginning of treatment. The administration of sulfanilamid seemed definitely to check the progress of this disease.

REPORT OF CASES

The patients failing to respond to sulfanilamid treatment presented clinical courses as follows:

CASE 1.—A 20-year-old unmarried white woman suffering from gonorrheal cervicitis and subacute pelvic inflammatory disease was given a total of 75 grams over a period of eight weeks. Only an occasional negative smear was obtained, and she did not remain free from demonstrable gonococcus infection longer than two weeks at a time. The drug was well tolerated and there were no significant changes in the blood picture except that the white count, which was elevated at the beginning of treatment because of the inflammatory process, returned to normal when this condition subsided.

* * *

CASE 2.—A 23-year-old married American Indian with acute gonorrheal cervicitis, skenitis, and bartholinitis, complicated by lues and a two months' pregnancy, was given a course of small doses of sulfanilamid aggregating fifteen grams. The smears remained positive throughout treatment, though the discharge improved. A course of large doses was begun, but the drug was poorly tolerated and the patient discontinued the treatment. Her smears are still

positive, and she is now being treated with local applications and douches.

CASE 3.—A 22-year-old unmarried white woman with acute gonorrheal skenitis and cervicitis, and a mild pelvic inflammatory process was treated with small doses of sulfanilamid, after which much improvement in symptoms was noted. The smears, however, remained positive. She was then given two courses of the large doses, which were very well tolerated. After the first course the smears were negative for about two weeks, but they again became positive and have remained so in spite of the second course of large doses. The patient is now being treated with local applications and douches.

CASE 4.—A 23-year-old unmarried white woman with acute gonorrheal cervicitis and skenitis was given small doses of sulfanilamid. Her smears became negative for a short time after treatment, but did not remain so. Following a subsequent course of large doses the smears again became negative and have remained negative for more than four weeks.

COMMENT

No serious reactions were noted in any of the patients. Those receiving the large doses frequently complained of malaise, dizziness, headache, nausea, and occasional vomiting. Initial cyanosis was common, but disappeared quickly when the dose was reduced. Skin rashes did not occur in any instance. The blood picture of the patients treated with small doses showed no appreciable changes, but a definite lowering of 10 per cent or more in hemoglobin content was noted in five patients (20 per cent), who were given the large doses. The greatest drop in hemoglobin was 25 per cent, which occurred fourteen days after treatment was begun.

A comparison of end results in the two groups using different dosages shows no material difference, which suggests that the large doses are not essential in all cases. Of the three failures in the small dosage group, only one was cured by a subsequent course of large doses.

The relatively high incidence of relapses brings up the question of the length of the treatment period. Dees and Colston[6], in their report of December, 1937, suggested a considerable extension of time in order to prevent relapses. Their hypothesis is that all the organisms are not killed in the initial days of treatment, and that after medication is discontinued, the remaining gonococci gradually increase in number until they can again be demonstrated clinically. This suggestion is in keeping with the findings of Long and Bliss in their experiments on mice infected with streptococci.

IN CONCLUSION

Our observations on the use of sulfanilamid in the treatment of gonorrhea in women confirm previous reports of its use in men. The prompt response to the drug, the facts that complications have not occurred and the infection has not progressed, and the apparent low toxicity of sulfanilamid lead us to conclude that this drug is of great value in the treatment of this type of infection.

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DISCUSSION

NORMAN H. WILLIAMS, M.D. (1052 West Sixth Street, Los Angeles).—Sulfanilamid is a two-edged sword—on the one hand there are undesirable reactions, on the other a potency against certain types of infection. As yet the method of its action is uncertain—whether its action incites increased resistance on the part of the body as, for instance, phagocytosis, whether it acts as a germicide, or whether a bacteriostatic agent, seems as yet undetermined. Whatever may be the action, however, the gonococcus is one of the organisms that is affected. This paper by Doctor Manor, as well as the work of others, has definitely shown improvement or cure in the majority of cases suffering from acute gonorrhea. The chronic cases are often improved clinically, but the pathology may remain. This may be no indication that the organisms do not disappear, often chronic adnexal pathology is sterile. The fire of a burning house may be extinguished, but the damage done remains. So few cases of gonorrheal joints and endocarditis treated with sulfanilamid have been reported, it still remains to be discovered to what extent the treatment may influence these conditions.

In more recent years reports have been issued concerning the use of the compliment-fixation test in gonorrheal infection. As the antigen has become more stabilized, the test seems to assume more diagnostic accuracy. Would it not be interesting to continue this excellent type of investigation by treating a series of known positive fixation cases, both acute and chronic, with sulfanilamid, studying particularly the effect of the latter, not only from the clinical standpoint, but especially changes, if any, to the degree of fixation.

THE LURE OF MEDICAL HISTORY†

ROCKEFELLER, OSLER AND WELCH

By EDGAR LORRINGTON GILCREEST, M.D.
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IN the death of John D. Rockefeller medicine lost the greatest lay benefactor it has ever had or probably ever will have. During his lifetime he both made and gave away more than any man who ever lived—over half a billion dollars. Up to 1934 the official figures reached the colossal sum of $530,853,632. He early learned that his philanthropies should be made through great channels, each set up to play a definite part in contributing to a planned investigation for an improved civilization. I have computed, from his various donations, that medicine was the recipient, directly or indirectly, of about $450,000,000. Because of these contributions, James Harvey Robinson placed

†A Twenty-Five Years Ago column, made up of excerpts from the official journal of the California Medical Association of twenty-five years ago, is printed in each issue of CALIFORNIA AND WESTERN MEDICINE. The column is one of the regular features of the Miscellany department, and its page number will be found on the front cover.